

REMARKS

The Applicants thank the Examiner for his careful analysis of the specification and claims. The Applicants have amended the claims as shown above and submit that the application is now in a proper form for allowance.

The Applicants have amended the title to more clearly reflect the subject matter claimed after restriction of the claims. The Applicants submit that the amendment does not constitute new matter.

The Applicants have amended paragraph 0017 to correct typographical errors that are obvious. The Applicants submit that the amendment does not constitute new matter.

The Examiner has rejected claims 1-6 and 8 under 35 U.S.C. 112, paragraph 2 for being indefinite and failing to particularly point out and distinctly claim the matter that the Applicants regard as the invention. Claims 1 and 8 have been substantially amended to increase clarity and comply with the requirements of 35 U.S.C. 112, paragraph 2. Therefore the rejection is traversed.

A trainable system is defined in paragraph 0020 of the instant application. It is a system that "can "learn" to determine patterns and that will allow for prediction of outcomes, upon analysis of unknowns similar to those in the training set." In the instant invention, "a training set" teaches "the trainable system about biomolecular interactions by providing examples of how proteins interact with each other by providing a number of examples of protein-protein interactions." (paragraph 0024). This process is described in more detail in Example 2 and supported in the computer appendix which is incorporated into the specification by reference.

The Examiner has rejected claims 1-8 for both anticipation and obviousness under 35 USC § 102 and § 103, respectively in view of Brauheim. The Examiner has further rejected all of the claims for obviousness in view of the admitted prior art. The Applicants submit that the instant invention is clearly distinct from the teachings of both Brauheim and the admitted prior art, which will be addressed independently.

The Applicants submit that there are at least three substantial differences between the instant invention as now claimed and the teachings of the Brauheim patent.

1. The Brauheim patent is neural network specific;
2. The Brauheim patent requires a 3-dimensional surface or geometric data inputs;
and
3. The Brauheim patent predicts binding energy exclusively.

The claims to the instant invention are directed to the use of support vector machines, taught in the specification to be superior to other trainable systems in Example 2; using primary sequence information; to predict biomolecular binding without requiring a prediction of binding energy. Therefore, the instant invention is clearly distinguished from the teachings of the Brauheim reference.

The use of primary structure information, rather than tertiary structural information, is a substantial advantage of the invention over the prior art. The use of primary structures is discussed in the first paragraph of the summary of the invention, paragraph 0013. The advantages of using primary sequence data are discussed in paragraph 0014. Primary structure is defined in paragraph 0023. One of the main advantages is that primary structure information (e.g. amino acid sequence) is available for far more proteins than structural information. This advantage becomes increasingly important because of the amount of primary sequence data being derived from the various genome programs. Moreover, the use of primary sequence data also allows for the prediction of interactions of membrane proteins which are notoriously difficult to analyze structurally. Therefore, the method of the instant invention can be used for the prediction of interactions between far more proteins.

The Brauheim method uses neural networks that are "trained to recognize the quantum mechanical electrostatic potential and geometry at the entire van der Waals surface of a group of training molecules and to predict the strength of interactions, or free energy of binding." (col 2, ln 19-22). Brauheim states that in his method "The entire

surface of each molecule, represented by a discrete collection of points, serves as the input to the neural network. In this way the invention utilizes quantum mechanical means to describe the molecular activity of a compound of interest.” Therefore, Brauheim sees the use of the 3-dimensional surface as an advantage of his invention. Therefore, it would not be obvious to modify the method of Brauheim to use primary sequence data to predict interactions.

The instant invention predicts interactions based on meeting a specific threshold rather than by predicting a binding energy. Therefore the determination of an interaction is binary, either meeting the threshold or not, as opposed to determining a binding energy for the pairing. One would not be motivated to modify Brauheim to produce such a binary result.

In view of these substantial differences between the claims of the instant invention and the teachings of Brauheim, the Applicants submit that claims 1-6 and 8 are clearly distinguished from the teachings of Brauheim; therefore, the rejections for anticipation and obviousness under 35 USC § 102 and 103 are traversed.

The Examiner has stated that the claims of the instant invention are obvious in view of the admitted prior art. The Examiner has made no specific comments regarding the application of the references to the claims. Therefore, the response made to the rejection concerns broad concepts, rather than specific, detailed responses. The Applicants request that if the Examiner deems the response insufficient that he make more specific rejections in the future to allow the Applicants to make a more appropriate response.

The Applicants submit that none of the references cited in the specification suggest or make obvious the method of the invention for the reasons detailed below.

Champion (2001), Fields and Song (1989) and McBeath and Schreiber (2000) all require the use of proteins and determination of interactions by contacting proteins with each other. This is clearly distinct from the computational method of the instant invention.

Enright (1999) requires that gene fusion events can be identified using a fusion

detection algorithm as a step to predict protein-protein interactions. This requires the use of whole genomes, which is either not possible, or at least impractical for most higher organisms.

Joachims (1999), Schoelkopf (1999) and Vapnik (1995) teach support vector machines for any use and do not include any teachings regarding protein-protein interactions.

Sankoff (1992), and Tekaia (1999) are concerned with evolution rather than protein-protein interactions, and require substantial amounts of genomic sequence information from multiple organisms to perform their analysis. This is distinct from the instant invention that can use any of a number of possible training sets.

Woese (1990) proposes a new phylogenetic tree, but does not propose a method for analysis of macromolecular interactions.

The Applicants submit that the claims of the instant invention are not obvious in view of the admitted prior art, either alone or in combination with each other, for the above reasons. Therefore, the rejection for obviousness under 35 USC § 103 is traversed.

The Applicants have added a number of claims. Support for all of the claims can be found in the specification and in the computer appendix that is incorporated by reference into the specification.

Claims 9 and 17 are supported by paragraph 0066. Claim 10 is supported, by section in (a) in Example 3, (b) paragraphs 0033 and 0038, (c) paragraph 0039, (d-e) the computer appendix, (f) paragraph 0039, (g) paragraphs 0042-3 and (h) the computer appendix. Claims 11-15 parallel claims 2-6. Claim 16 is supported by the computer program. Claims 18 is supported by paragraph 0027. The Applicants submit that these claims are both novel and non-obvious in view of the prior art.

FEES

The Applicants have authorized the Commissioner to charge the Deposit Account

indicated the amount of \$475 to cover the fees for a request for a three month extension. It is believed that no additional fee is due. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account 50-1990, referencing case number BUCSD 1025958.

CONCLUSIONS

In view of the forgoing amendments and arguments, the Applicants submit that the application is now in proper form for allowance. However, if there are any outstanding issues remaining in the case that can be resolved by telephone, the Examiner is encouraged to call the Agent for Applicant below, collect, to discuss the outstanding issues.

Respectfully submitted,

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